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Original Article

Anticyclic modulated ventilation versus continuous positive airway pressure in patients with coexisting obstructive sleep apnea and Cheyne–Stokes respiration: a randomized crossover trial

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ABSTRACT

Background: Although coexisting obstructive sleep apnea (OSA) and Cheyne–Stokes respiration (CSR) occur frequently in patients with heart diseases, optimal treatment remains unclear. Positive airway pressure (PAP) effectively treats OSA and adaptive servo-ventilation (ASV) has been shown to improve CSR. We compared a new treatment algorithm combining automatic continuous positive airway pressure (APAP) and ASV (anticyclic modulated ventilation, ACMV) versus continuous positive airway pressure (CPAP).

Methods: Thirty-nine patients (35 male, four female; aged 65.5 ± 9.7 years; body mass index, 31.0 ± 5.9 kg/m^2) with underlying heart disease and coexisting OSA and CSR were enrolled. After diagnostic polysomnography (PSG) and CPAP titration, patients were randomized either to CPAP or to ACMV for four weeks of treatment in a crossover design.

Results: Total apnea–hypopnea index (AHI) was 49.0 ± 18.8/h at baseline, 12.3 ± 14.6/h with CPAP ($P < 0.001$ vs baseline), and 3.7 ± 5.6/h with ACMV ($P < 0.001$ vs baseline and vs CPAP). Obstructive AHI was 20.7 ± 14.4/h at baseline, 5.1 ± 9.3/h with CPAP ($P < 0.001$ vs baseline), and 0.4 ± 0.4/h with ACMV ($P < 0.001$ vs baseline and vs CPAP). Central AHI was 28.3 ± 13.4/h at baseline, 7.2 ± 9.7/h with CPAP ($P < 0.001$ vs baseline) and 3.3 ± 5.4/h with ACMV ($P < 0.001$ vs baseline and vs CPAP). Ejection fraction was increased significantly (from 38.6 ± 15.6 to 44.4 ± 12.2%) only with ACMV. Subjective sleepiness significantly improved only with CPAP whereas objective sleep quality and treatment adherence were not different between both treatment modalities.

Conclusion: ACMV is an effective treatment option in patients with coexisting OSA and CSR. It is superior to CPAP in reducing total AHI as well as obstructive and central AHI.

1. Introduction

Sleep-disordered breathing is a major challenge in patients with chronic heart failure (CHF) due to ischemic heart diseases, dilated cardiomyopathy or arterial hypertension, affecting up to 50% of those patients [1]. Although pure Cheyne–Stokes respiration (CSR) is predominantly found in CHF patients with a left ventricular ejection fraction (EF) <45%, a substantial proportion of patients with stable heart failure also suffers from coexisting obstructive sleep apnea (OSA) [1–3]. Until now, the optimal treatment of patients presenting with both CSR and OSA has remained unclear.

For many years, continuous positive airway pressure (CPAP) has been the treatment of choice for OSA [4]. Moreover, recent studies have demonstrated that CPAP improves heart function and quality of life in CHF patients with OSA [5,6] and reduces the amount of CSR up to 50% [7]. Auto-adjusting CPAP (APAP) is a technical variation of CPAP designed to detect respiratory events and to adapt the pressure according to the actual need of the patient, thereby reducing the treatment pressure [8–10].

Adaptive servo-ventilation (ASV), on the other hand, has been demonstrated effectively to suppress central respiratory events in CHF patients with CSR [11] and to be superior to oxygen alone or

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CPAP [12]. However, whereas in some studies left ventricular function improved significantly with ASV [13,14], other studies failed to demonstrate a beneficial effect of ASV on echocardiographic parameters or exercise performance [15].

Recently, we published a pilot study evaluating a new mode of positive airway pressure treatment in patients with coexisting CSR and OSA [16]. This anticyclic modulated ventilation (ACMV) device, combining an adaptive servo-ventilation mode and an automatic positive airway pressure algorithm, effectively reduced obstructive respiratory disturbances as well as central respiratory events over a two-week treatment period [16]. Therefore, the aim of the present study was to compare ACMV with fixed CPAP therapy in patients with underlying heart disease and coexisting obstructive and central sleep apnea.

2. Methods

2.1. Patients

For this study, patients were recruited from the sleep laboratory of Bethanien Hospital Solingen, a university-based center for sleep medicine and respiratory care. Patients with cardiac disease (coronary heart disease, arterial hypertension, dilated cardiomyopathy) and an apnea–hypopnea index (AHI) >15/h with a proportion of >20% central or periodic disturbances were eligible. Exclusion criteria were acute myocardial infarction, unstable angina pectoris, cardiac surgery within the previous three months, and New York Heart Association (NYHA) heart failure class IV. Optimal medical treatment of the underlying cardiovascular disease had to be reached prior to inclusion. The study was approved by the ethics committee of the University of Witten/Herdecke (approval number 13/2008) and all patients gave their written informed consent (ClinicalTrials.gov identifier: NCT00811668).

2.2. Study design

A randomized, operator- and patient-blinded, single-center crossover study was performed including a washout period between the two treatment periods. Fig. 1 gives an overview of the study design. After baseline polysomnography patients were randomized (lots were drawn by a person not involved in the study) to start treatment either with fixed CPAP or with ACMV. Patients and data analysts were blinded to therapy allocation. All patients performed a manual CPAP titration night to determine optimal CPAP pressure for fixed CPAP therapy and to adjust the pressure profile of the ACMV device. In the ACMV mode, the lower limit of the end-expiratory positive airway pressure (EEPAP, see below) was set between 6.0 and 10.0 cmH_2O according to the optimal CPAP pressure obtained by the manual titration procedure and the maximum inspiratory positive airway pressure (IPAP) was set to 20 cmH_2O. In four patients who did not tolerate this maximum pressure, IPAP was limited to a maximum of 15 and 16 cmH_2O, respectively. All patients were treated with automatic back-up frequency. In all patients accurate mask fitting and training phases during the daytime were performed. After a four-week treatment period, patients were re-evaluated polysomnographically and then the treatment mode was changed. The first night with the new mode was performed in the sleep laboratory. After a washout period of one week and the second treatment period of four weeks, patients again performed an in-hospital polysomnography. No supplemental oxygen or humidification was applied. At baseline and after each treatment period, two-dimensional echocardiography was performed to determine EF using apical four- and two-chamber views and the modified Simpson method. Treatment adherence, expressed as hours/night usage, was determined by reading out the device-immanent software.

2.3. Outcome variables

Primary endpoints were the total number of respiratory events (total AHI) as well as the obstructive AHI and the central AHI. Secondary endpoints were sleep quality, the change in EF, and treatment adherence.

2.4. Anticyclic modulated ventilation

For ACMV we used the device SOMNOventCR® (Weinmann, Hamburg, Germany). The ACMV mode was described in detail previously [16]. Briefly, it combines an automatically adjusting CPAP (APAP) mode and an adaptive servo-ventilation. The device applies

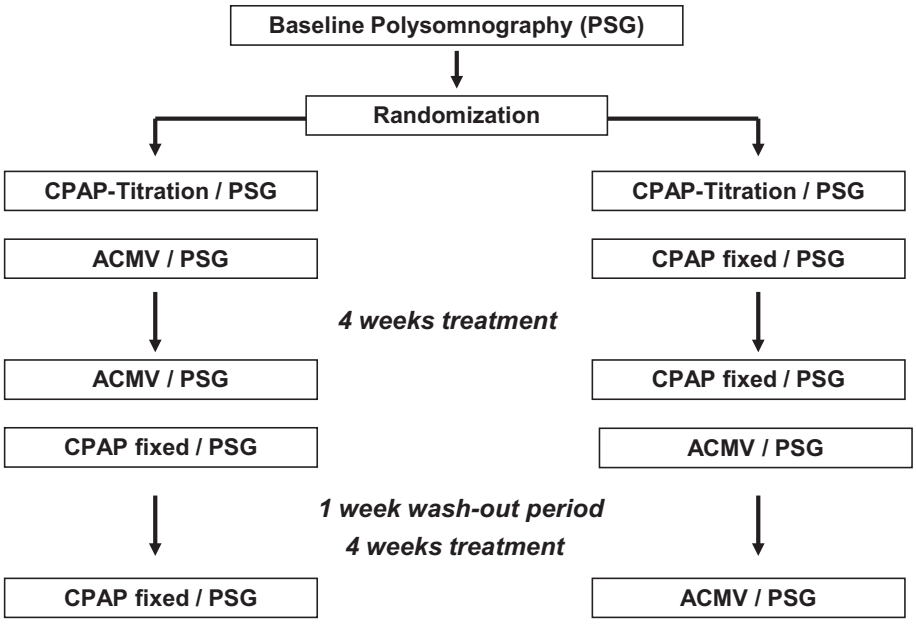

Fig. 1. Overview of study design. CPAP, continuous positive airway pressure; ACMV, anticyclic modulated ventilation.

three different pressure levels: the inspiratory positive airway pressure (IPAP), which represents the pressure level during inspiration, the expiratory positive airway pressure (EPAP), which represents the pressure level during early expiration and the end-expiratory positive airway pressure (EEPAP). Whereas the EPAP only serves as an exhalation relief during the initial period of expiration, EEPAP is the pressure achieved at the end of expiration and therefore it represents the positive pressure to keep the upper airway open. In case of pure obstructive events, the EEPAP is gradually increased in the manner of an automatic CPAP algorithm, whereas the IPAP remains on the same niveau as the EEPAP. In case of periodic breathing with decreasing tidal volume, ventilation is supported by increasing the difference between IPAP and EEPAP. Respiratory events are detected, based on the analysis of actual minute ventilation, flow profile, and snoring. The minute ventilation is compared with the average minute ventilation in a moving window. Obstructive and central events are discriminated based on the recognition of flattening of the flow curve and on the reaction on additional pressure support. During apneas, mandatory breaths are applied automatically depending on the baseline respiratory frequency of the patient (automatic back-up frequency).

2.5. Polysomnography

In-laboratory polysomnography was performed using the Alice 4® Sleep Diagnostic System (Respironics, Murrysville, PA, USA) and the SOMNOLab® (Weinmann). The following parameters were recorded: electroencephalogram C4A1 and C3A2, submental electromyogram, electro-oculogram, thoracic and abdominal efforts (piezo plethysmography), respiratory flow (nasal pressure signal), snoring signal (laryngeal microphone), oxygen saturation (finger pulse oximetry), and pretibial electromyogram. Sleep stages and arousals were analyzed in accordance with the guidelines of Rechtschaffen and Kales [17]. Arousals were defined as respiratory-related when they occurred during or up to 2 s after an apnea or hypopnea, or in case of periodic breathing, when they occurred during hyperventilation. Apnea was defined as the cessation of respiratory flow for $\geqslant$10 s. Hypopnea was defined as a reduction in nasal pressure signal (flow) of $\geqslant$50% for $\geqslant$10 s accompanied by an arousal or decrease in oxygen saturation of $\geqslant$3%. Central apneas were scored if respiratory efforts were absent. Central hypopneas were scored if there was a reduction in respiratory effort without flattening of the flow curve or paradoxical motion in the thoracic or abdominal channels as previously described [18].

2.6. Statistics

Numeric variables such as anthropometric and polysomnography data were expressed as mean ± standard deviation. Calculations for significant differences between baseline measurements and each treatment mode and between the two treatment modes with rejection of the null hypothesis at $P < 0.05$ were carried out using the Wilcoxon test. *P*-values were not adjusted for multiplicity. Data analysis was performed in SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, USA).

3. Results

Thirty-nine patients participated in the study with no dropouts during the study period. Anthropometric data of the study population are summarized in Table 1. The predominant underlying cardiac disease among the patients was hypertension, most of them being in the NYHA classes I and II.

At baseline, total AHI was 48.4 ± 18.7 with an obstructive AHI of 20.9 ± 15.7 and a central AHI of 27.6 ± 12.9. With both treatment modes, total AHI was significantly reduced both after one night and after four weeks treatment to normal values. ACMV led to a further significant reduction of total AHI in comparison with CPAP. Both treatment modes significantly normalized obstructive respiratory events, but, with ACMV, significantly fewer obstructive events were detected. CPAP effectively suppressed central respiratory events to about one-third in the first treatment night and after four weeks whereas ACMV improved central AHI significantly better to <1/h (Table 2).

Table 1
Anthropometric data of the study population (n = 39).

Variable	Value
Age (years)	65.5 ± 9.7
Weight (kg)	95.6 ± 22.6
Height (cm)	174.2 ± 8.3
Body mass index (kg/m^2)	31.0 ± 5.9
Male sex (n)	35 (89.7%)
NYHA class	
I (n)	16 (41.0%)
II (n)	20 (51.3%)
III (n)	3 (7.7%)
Hypertension (n)	28 (71.8%)
Coronary heart disease (n)	7 (17.9%)
Cardiomyopathy (n)	1 (2.6%)
Other condition (n)	3 (7.7%)

NYHA, New York Heart Association.

Fig. 2 demonstrates the individual change of the total AHI. With CPAP a reduction to <10/h was achieved in about half of the patients, whereas with ACMV it suppressed total AHI <10/h in all but two patients.

After four weeks of treatment, polysomnography demonstrated no significant difference in total sleep time or in slow wave sleep, but there was a significant reduction in light sleep and an increase in REM sleep with both CPAP and ACMV, although no difference between the two treatment modes. Mean and minimal oxygen saturation and time spent below 90% oxygen saturation similarly improved with both treatment modes (Table 3).

Cardiac function improved with both therapy modalities, but the EF significantly increased only after ACMV therapy (Table 3).

Subjective sleepiness measured by ESS significantly decreased with CPAP, but not with ACMV. Treatment adherence was more than 6 h per night and not different between treatment modalities (Table 3).

Table 4 demonstrates the applied pressures with both devices. Whereas the mean pressure was 8.5 cmH_2O in the CPAP group, the mean EEPAP in the ACMV mode – corresponding to the CPAP – varied between 6.5 and 10.5 cmH_2O and the IPAP varied between 6.6 and 17.2 cmH_2O.

At the end of the study, 32 of 39 patients (82%) preferred ACMV for long-term treatment at home. Seven gave preference to conventional CPAP mode. Patients' choice was independent of the random order during the study.

4. Discussion

This randomized crossover study demonstrates that an ACMV device combining an adaptive servo-ventilation mode and an APAP algorithm effectively reduces obstructive respiratory disturbances as well as central respiratory events in patients with coexisting CSR and OSA. It is superior to conventional CPAP in diminishing respiratory events and is preferred by patients.

Sleep-disordered breathing, either CSR or OSA, is a major problem in patients with underlying cardiac diseases resulting in repetitive hypoxia, sympathetic nerve activation, arousals from sleep, ventricular arrhythmias, therefore affecting prognosis in these

Table 2
Sleep-disordered breathing parameters obtained by cardiorespiratory polysomnography at baseline and during CPAP and ACMV.

Parameters	Baseline	CPAP 1st night	CPAP 4 weeks	ACMV 1st night	ACMV 4 weeks
AHI total (/h)	48.4 ± 18.7	13.6 ± 11.8[a]	13.6 ± 13.5[a]	3.1 ± 3.8[a,b]	3.3 ± 4.5[a,b]
AHI obstructive (/h)	20.9 ± 15.7	5.5 ± 9.4[a]	4.2 ± 7.1[a]	0.6 ± 1.3[a,b]	0.3 ± 0.4[a,b]
AHI central (/h)	27.6 ± 12.9	8.1 ± 9.0[a]	9.4 ± 10.5[a]	2.4 ± 1.3[a,b]	3.0 ± 4.3[a,b]
AI total (/h)	25.4 ± 18.3	7.0 ± 10.5[a]	7.0 ± 11.4[a]	0.5 ± 1.3[a,b]	0.3 ± 0.5[a,b]
AI obstructive (/h)	13.6 ± 13.1	4.3 ± 9.2[a]	3.3 ± 6.6[a]	0.3 ± 0.9[a,c]	0.2 ± 0.3[a,c]
AI central (/h)	11.9 ± 12.6	2.7 ± 5.7[a]	3.8 ± 8.0[a]	0.3 ± 0.6[a,b]	0.1 ± 0.4[a,b]
HI total (/h)	23.0 ± 13.9	6.6 ± 7.5[a]	6.6 ± 7.5[a]	2.6 ± 3.1[a,c]	3.0 ± 4.3[a,c]
HI obstructive (/h)	7.3 ± 6.3	1.2 ± 1.9[a]	0.9 ± 2.0[a]	0.4 ± 1.0[a,c]	0.2 ± 0.3[a,c]
HI central (/h)	15.7 ± 12.2	5.4 ± 7.4[a]	5.6 ± 6.7[a]	2.2 ± 3.0[a,c]	2.9 ± 4.2[a,c]
Arousals total (/h)	35.1 ± 17.5	17.1 ± 11.6[a]	18.6 ± 11.6[a]	12.9 ± 7.7[a,d]	14.3 ± 8.8[a,d]
Arousals respiratory (/h)	19.9 ± 18.9	4.3 ± 5.1[a]	4.8 ± 6.7[a]	1.6 ± 4.7[a,b]	1.0 ± 1.4[a,b]

CPAP, continuous positive airway pressure; ACMV, anticyclic modulated ventilation; AHI, apnea–hypopnea index; AI, apnea index; HI, hypopnea index.
[a] $P < 0.001$ vs baseline.
[b] $P < 0.001$ vs CPAP.
[c] $P < 0.01$ vs CPAP.
[d] $P < 0.05$ vs CPAP.

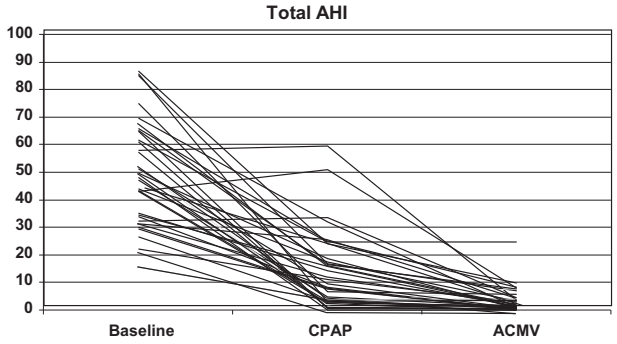

Fig. 2. Individual change of the apnea–hypopnea index (AHI) with continuous positive airway pressure (CPAP) and anticyclic modulated ventilation (ACMV).

Table 3
Sleep parameters, ejection fraction, ESS and treatment adherence during CPAP and ACMV.

Parameters	Baseline	CPAP 4 weeks	ACMV 4 weeks
TST (min)	323.4 ± 73.0	289.4 ± 62.8	291.2 ± 61.4
N1/N2 (min) (%TST)	229.4 ± 56.3 (70.9)	183.8 ± 53.7 (63.7)[a]	180.7 ± 43.2 (62.2)[b]
N3 (min) (%TST)	50.8 ± 41.2 (15.8)	45.4 ± 32.1 (15.6)	55.3 ± 29.4 (18.9)
REM (min) (%TST)	43.1 ± 29.1 (13.3)	60.1 ± 31.0 (20.8)[b]	55.1 ± 22.1 (18.9)[b]
SaO_2 min (%)	77.1 ± 9.3	84.6 ± 4.9[b]	84.5 ± 3.5[b]
SaO_2 mean (%)	92.6 ± 2.2	94.5 ± 1.8[b]	94.2 ± 2.1[b]
SaO_2 <90% (min)	53.9 ± 55.6	9.9 ± 29.1[b]	5.0 ± 10.0[b]
Ejection fraction (%)	38.6 ± 15.6	42.0 ± 13.1	44.4 ± 12.2[a]
ESS	8.4 ± 4.3	5.9 ± 3.4[b,c]	7.1 ± 3.8
Adherence (h/night)		6.4 ± 1.2	6.3 ± 1.5

ESS, Epworth Sleepiness Scale; CPAP, continuous positive airway pressure; ACMV, anticyclic modulated ventilation; TST, total sleep time; N1/N2/N3, stage 1/2/3 sleep time; REM, rapid eye movement sleep; SaO_2, arterial oxygen saturation.
[a] $P < 0.05$ vs baseline.
[b] $P < 0.001$ vs baseline.
[c] $P < 0.001$ vs ACMV.

Table 4
Applied pressures in the CPAP and ACMV mode.

	Mean	Min	Max
CPAP (cmH_2O)	8.5 ± 1.7		
EPAP (cmH_2O)	6.2 ± 1.3	4.2 ± 0.7	9.1 ± 1.6
EEPAP (cmH_2O)	8.9 ± 1.3	6.5 ± 2.2	10.5 ± 1.4
IPAP (cmH_2O)	10.1 ± 1.5	6.6 ± 2.1	17.2 ± 2.4

CPAP, continuous positive airway pressure; ACMV, anticyclic modulated ventilation; EPAP, expiratory positive airway pressure; EEPAP, end-expiratory positive airway pressure; IPAP, inspiratory positive airway pressure.

patients [18–23]. Whereas CPAP is the treatment of choice in OSA, its role in the therapy of CSR remains unclear. In the CANPAP trial, CPAP failed to demonstrate a positive effect on heart transplant-free survival in CHF patients [7]. However, a post-hoc analysis suggested that CPAP might improve cardiac function and transplant-free survival in those patients for whom CSR is suppressed soon after initiation [24]. Bilevel positive airway pressure might even worsen CSR and non-CSR central apneas, and therefore plays only a minor role in the treatment of sleep-disordered breathing in heart failure patients [25]. Since its introduction in 2001, adaptive servo-ventilation has been shown effectively to suppress central respiratory events and improve cardiac function in patients with pure CSR [12,14,26]. However, in clinical practice, many patients with cardiac diseases do not have pure OSA or pure CSR but rather a combination of both with varying predominant respiratory disturbances that may even change during the same night [27].

The ACMV device used in this study focuses on this patient group with coexisting OSA and CSR, combining an automatic CPAP and an adaptive servo-ventilation, and has demonstrated efficacy in a short-term pilot study [16]. To the authors' knowledge, this is the first study comparing the specific ACMV algorithm with CPAP in patients with coexisting OSA and CSA.

In the present study, ACMV effectively reduced central respiratory events to <5/h sleep after four weeks of treatment, which is comparable to previous studies in patients with CSR [11,26,28] or central sleep apnea [29], using different adaptive servo-ventilation devices. CPAP alone even lowered central AHI to one-third, which is surprisingly better than in the CANPAP trial, demonstrating a reduction of central respiratory events only by 50% in the CPAP group [7]. Probably this discrepancy is due to the different study population. While the CANPAP trial, included patients with pure or predominant CSR, in the present study patients with more pronounced obstructive events were recruited. However, although

in the present study CPAP reduced central respiratory events by a greater amount, there was a further significant reduction by the ACMV device.

Unexpectedly ACMV also was superior to CPAP alone in reducing obstructive respiratory events. In the present study we compared a fixed CPAP device with a device including an automatic CPAP algorithm. Auto-adjusting CPAP has been shown to be equally effective as fixed CPAP, thereby reducing the mean CPAP pressure [30]. Although we performed a manual CPAP titration to determine optimal CPAP pressure for fixed CPAP therapy, it cannot be excluded that under certain conditions the determined fixed CPAP pressure was not sufficient to prevent all obstructive events. This is supported by the fact that in the ACMV group the mean EEPAP, which corresponds to the CPAP, was slightly higher than the mean CPAP in the CPAP group (8.9 vs 8.5 cmH_2O) and varied between 6.5 and 10.5 cmH_2O. In addition, three patients demonstrated a relevant mask leakage on CPAP in spite of accurate mask-fitting resulting in an obstructive AHI >10/h.

In the present study, the mean inspiratory pressure to overcome hypoventilation phases due to CSR varied between 6.6 ± 2.1 and 17.2 ± 2.4 cmH_2O. It could be speculated that the numerous pressure variations during the night conducted by the ACMV algorithm would lead to more arousals and poorer sleep quality, but this did not occur. The frequency of arousals was even lower with ACMV and total sleep time did not differ between the two treatment modes. In automatic CPAP therapy for OSA, also performing a considerable number of pressure variations, substantial arousals are not induced in the vast majority of patients, but only in some individuals [31]. However, in our study most of the patients voted for the ACMV mode, when asked about their preference after both treatment periods, and only 18% preferred the fixed CPAP mode. In addition, treatment adherence – which was notably high – was nearly the same with both treatment modalities. The mean EPAP level during early expiration, which works as an exhalation relief, was 2.7 cmH_2O lower than the mean EEPAP. It may be speculated that this tool influenced the patients' preference decision.

Surprisingly, subjective sleepiness after four weeks of treatment was significantly lower with CPAP in comparison with ACMV, although sleep parameters and arousals did not differ and respiratory events were even better suppressed with ACMV. However, most of the patients were not sleepy at baseline, which is a well-known phenomenon in CHF patients. Therefore, ESS is probably not an adequate instrument to determine sleepiness in this population.

Some previous studies in CHF patients demonstrated that adaptive servo-ventilation improves cardiac function. Philippe et al. found a significant increase in left ventricular EF only with ASV, not with CPAP [26], and in the study by Oldenburg et al. patients treated with ASV had an absolute increase in EF of about 4% after six months [14]. In the present study, CPAP therapy improved EF from 38.6 ± 15.6 to 42.0 ± 13.1, which is comparable to a previous study also focusing on patients with coexisting OSA and CSR [13]. Sin et al. found a substantially greater increase in EF in their CPAP-treated CHF patients, but they included only patients with pure CSR and a considerably lower EF at baseline [32]. However, in our study only ACMV led to a significant increase in EF after four weeks of treatment.

This study compared ACMV with CPAP, not with APAP, for two reasons. First, in Germany CPAP with a fixed pressure – not with APAP – is still the preferred treatment for sleep-disordered breathing in many sleep laboratories, and many insurance companies ask for a CPAP trial before approving assumption of costs for an adaptive servo-ventilation device. Secondly, pure APAP is not recommended for heart failure patients with CSR. However, to determine the additional effect of the APAP algorithm in the ACMV device, one had to compare ACMV with an APAP device.

There are some other limitations of the present study. The first limitation refers to the study population. Because we focused on patients with coexisting OSA and CSR, but not on more severely ill patients with overwhelming CSR, most of the patients in our study were in a lower NYHA classification. However, because this targeted patient group is relevant in daily practice, in our opinion it is necessary to search for treatment options for this population. The results of the present study therefore may not apply to other patient groups – for example, patients with poor CSR or more severe heart failure, or patients with central sleep apnea of other origin. The second limitation refers to the short study length of only four weeks of treatment. However, because significant treatment effects on respiratory disturbances and sleep quality were already observed after four weeks of treatment, it is likely that the results of the study are also valid for long-term therapy. Third, blinding of all data was not possible because of the different algorithm of both treatment modes. However, the sleep physicians and statisticians who scored the polysomnography tests and analysed the data were completely blinded to the treatment assignment. The fourth limitation is the difficulty in differentiating between obstructive and central hypopneas. Although we used a distinct algorithm to score a hypopnea either as obstructive or as central [18], in the absence of an esophageal pressure signal – which is not feasible in daily practice – it cannot be excluded that some obstructive hypopneas were wrongly characterized as central or vice versa. However, because this would have been the case with both treatment modes, we believe that this did not influence the results of the study.

In conclusion, this study demonstrated that ACMV combining automatic CPAP and adaptive servo-ventilation is an effective treatment option and superior to conventional CPAP in patients with coexisting OSA and CSR. It may possibly improve cardiac function. However, these results need to be confirmed in larger randomized controlled trials powered to detect a benefit in mortality with this treatment mode.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.02.012.

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